

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Chief Technology Officer (OCTO)

Announcement of Requirements and Registration for ‘KidneyX: Redesign Dialysis’

Authority: 15 U.S.C. 3719

The Kidney Innovation Accelerator (KidneyX) is a partnership between the U.S. Department of Health and Human Services (HHS) and the American Society of Nephrology (ASN). HHS and ASN plan to hold a series of KidneyX prize competitions to develop innovative solutions that can prevent, diagnose, and/or treat kidney diseases. Prize competitions challenge individuals, communities, businesses, institutions, and non-profit organizations to achieve defined goals in a defined timeframe. In KidneyX prize competitions, HHS and ASN plan to offer cash prizes and other incentives to increase the number and variety of problem-solvers addressing critical issues in kidney health. Every KidneyX prize competition will define a problem, without a pre-conceived notion of what the solution(s) should be, and ask participants to find solutions. Think better, think bold, think big.

Through this notice, HHS is announcing KidneyX’s initial prize competition, KidneyX: Redesign Dialysis, which will run in two phases. Phase 1 asks participants to design potential solutions or components of solutions, while Phase 2 asks for the demonstration of a prototype solution or component. Both phases will be open to all eligible participants (i.e., participants do not have to submit a Phase 1 entry in order to submit a Phase 2 entry). This prize competition is being run under the authority of Section 24 of the Stevenson-Wydler Technology Innovation Act of 1980 (15 U.S.C. 3719), as added by the America COMPETES Reauthorization Act of 2010 (Pub. L. 111–358).

HHS reserves the right to change or update this notice at any time, including subsequent to the announcement of the results of Phase 1 of the prize competition.

Dates for KidneyX: Redesign Dialysis, Phase 1

Submission period begins: October 25, 2018

Submission period ends: February 28, 2019, 5:00 p.m. ET

Awardees announced by: April 30, 2019

Dates for KidneyX: Redesign Dialysis, Phase 2

Submission period begins: April 30, 2019

Submission period ends: January 31, 2020, 5:00 p.m. ET

Awardees announced by: March 27, 2020

Sections of this announcement:

- A. Background
- B. Subject of Prize Competition
- C. Prize Competition Structure
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- E. Submission Rules, Judging Criteria, Eligibility, and IP Rights
- F. Technological and Scientific Needs in Potential Renal Replacement Therapies

A. Background

Over 700,000 adults in the U.S. have kidney failure, also called End Stage Renal Disease (ESRD), a debilitating condition that is quickly fatal without treatment. To survive, people with ESRD must receive some form of renal replacement therapy. For more than half a century, people with kidney failure have had only one treatment option other than a kidney transplant: dialysis.¹ Dialysis, a type of renal replacement therapy, clears excess fluid and filters out some of the toxins that the kidney normally excretes, but dialysis replicates only the kidney's filtration function, and only while the patient is on dialysis. Dialysis is a life-saving technology, but it still leaves patients with substantial morbidity, mortality, and a decreased quality of life.

Most dialysis in the United States is performed in hemodialysis units, where patients with kidney failure are connected to machines for three to five hours, three times a week. Some advances on in-clinic dialysis have occurred, including home treatment and peritoneal dialysis, but key limitations of in-center dialytic therapy as currently practiced include its intermittent nature, the need for patients to travel to receive treatment, and the failure to restore other kidney functions besides filtration clearance.

Kidney transplantation can extend lifespan and improve quality of life, but the number of kidney donations is not remotely close to meeting the current demand. Furthermore, while kidney transplantation best duplicates native kidney function, the potential for organ rejection is ever present, requiring life-long immunosuppression with its risks of life-threatening infections and the need for multiple medications.

Treatment of ESRD is extremely expensive for the Federal government: Medicare alone spends more than \$34 billion per year for beneficiaries with ESRD.² Despite the high cost of dialysis treatment, dialysis patients' 5-year life expectancy is worse than that of most cancer patients.³ Alternatives to current renal replacement therapies for people with ESRD are long overdue.

B. Subject of Prize Competition

The KidneyX: Redesign Dialysis prize competition seeks solutions or components of solutions that offer patients significant alternatives to dialysis as it is generally practiced today. The competition is intended to attract a wide range of ideas and participants and thus to catalyze development of new, improved classes of renal replacement therapeutic options. The goal is not necessarily to build a better dialysis machine or to provide iterative improvements to dialysis: other possibilities may include constructs that do not resemble dialysis as it is currently practiced, but rather shift the paradigm for how kidney failure is managed. Of particular interest is applying advanced technologies currently used in non-kidney areas to current or potential

¹ Of American adults currently with ESRD, 200,000 have received kidney transplants, while 500,000 require chronic dialysis to survive. United States Renal Data System, *2017 USRDS Annual Data Report*, 6.

² United States Renal Data System, *2017 USRDS Annual Data Report*, https://www.usrds.org/2017/download/2017_Volume_1_CKD_in_the_US.pdf, 6.

³ Kirsten L. Johansen. "Life Expectancy Gains for Patients with ESRD," *Clin. J. Am. Soc. Nephrol.* 2018 13: 11-12; United States Renal Data System: *Epidemiology of kidney disease in the United States*, 2017; Centers for Disease Control and Prevention: *Cancer Survival Data: 5-Year Relative Survival by Selected Primary Site, Race, Sex, and Age Group*, 2017

renal replacement therapy technologies. Section D of this announcement provides more information about the scope of KidneyX: Redesign Dialysis.

This prize competition seeks ideas and participants from outside the field of kidney health as well as from within it. Section F of this announcement gives specific details about some current technological and scientific needs in renal replacement therapy. Many potential prize competition participants may have applicable technologies, concepts, or expertise from domains that have not previously been considered in improving renal replacement therapy. Similarly, there may be innovators working on component technologies or discrete concepts that may have utility as one part of a novel renal replacement therapy solution. As such, HHS and ASN encourage participation from participants with concepts for specific kidney replacement therapeutic options as well as participants who believe their concept might be a component in developing a successful renal replacement therapeutic option.

C. Prize Competition Structure

This prize competition will be run in two phases; participants may submit a solution in Phase 2 even if they did not participate in Phase 1. **Phase 1** is a design phase that asks participants to submit their ideas and solutions related to renal replacement therapy. Judges will review submissions, and an authorized official will select up to 15 Phase 1 winners from the submissions received (see Section E, below, for submission rules and judging criteria) (note: the HHS Chief Technology Officer will approve the distribution of HHS prize money, while an ASN representative will approve the distribution of ASN prize money). Each eligible Phase 1 winner will receive a \$75,000 cash prize and may be invited to present their ideas at an open public meeting with an audience expected to include stakeholders from across government, investors, patients, industry representatives, academics, and non-profit organizations. Eligibility rules are described in Section E.

Phase 2 of the prize competition asks participants to build their proposed solution into a prototype (submission and judging criteria are located in Section E, below). Participants may also submit a prototype solution in Phase 2 even if they have not submitted a design solution in Phase 1. At the end of Phase 2, judges will review submissions and an authorized official will select up to 3 winners, with each eligible winner receiving a cash prize of \$500,000 (note: the HHS Chief Technology Officer will approve the distribution of HHS prize money, while an ASN representative will approve the distribution of ASN prize money). Eligibility rules are described in Section E.

HHS and ASN will also help Phase 1 and Phase 2 winners receive input and feedback from investors, business and manufacturing experts, scientists, engineers, and others as needed. HHS plans to enable participants to interact with government representatives from the Food and Drug Administration (FDA), the Centers for Medicare & Medicaid Services (CMS), and the National Institutes for Health (NIH), who can provide feedback, to the extent appropriate for each agency. Please note that the participation of government entities is not a guarantee of any particular result (e.g., premarketing authorization approval or clearance by FDA, coverage or payment

under Medicare, or the award of an NIH grant).⁴

D. Prize Competition Scope

This prize competition seeks solutions that can replicate normal kidney functions and improve quality of life. Listed below are the areas that comprise the scope of this prize competition: solutions must address at least one of these areas. Additional details about current technical and scientific needs can be found in Section F of this document, as well as the [Kidney Health Initiative’s “Technology Roadmap for Innovative Approaches to Renal Replacement Therapy.”](#)

Replicating Kidney Functions:

- Blood Filtration (filtering blood to remove waste and excess fluid)
- Electrolyte Homeostasis (maintaining appropriate levels of key minerals in the blood)
- Fluid Regulation (regulating the amount of and/or removing excess fluid)
- Toxin Removal and Secretion (removing, limiting or preventing toxins in the bloodstream)
- Filtrate Drainage and Connectivity (removing excess filtrate after processing; connectivity issues for filtration, processing, and exterior drainage)

Improving Patient Quality of Life:

- Minimizing burden on the family and care partner(s)
- Improving ability to work, travel, and engage in recreational activities
- Increasing mobility and physical activity
- Improve upon vascular/peritoneal access to limit needle sticks, physical alterations to patient
- Reducing disease and treatment complications
- Providing more choices for treatment
- Liberalizing diet and fluid regulation
- Reducing medication burden

Improved renal replacement therapy access (vascular or peritoneal access needed for treatment)

Addressing engineering challenges (e.g., preventing clotting, bleeding, and infection in vascular circuit and associated devices)

Ancillary technologies

Biomaterials development

Biological and Immunological modulation

Biosensor development and other safety monitoring functions

⁴ Any such input provided by government entities would be made available to all participants on an equal basis, as well as to members of the public, consistent with applicable law and policy.

E. Submission Rules, Judging Criteria, Eligibility, and IP Rights

Amount and Payment of the Prize:

For the KidneyX: Redesign Dialysis prize competition, \$2,625,000 in total prize funds will be available. Phase 1 offers \$1,125,000 in total prize money, and Phase 2 offers \$1,500,000 in total prize money. HHS is contributing \$655,000 to the total prize pool and will pay 24.9% of each prize; ASN is contributing \$1,970,000 to the prize purse.

Prizes awarded under this prize competition will be paid by electronic funds transfer and may be subject to Federal income taxes. HHS and ASN will comply with the Internal Revenue Service withholding and reporting requirements, where applicable. Prizes offered by ASN will be paid directly by ASN to prize recipients, and prize money offered by HHS will be paid directly by HHS to prize recipients. If ASN fails to pay any portion of the monetary prize it has indicated it intends to pay, HHS does not have the legal authority to pay the amount on their behalf.

Phase 1 Submission Requirements:

For Phase 1, participants are asked to submit designs for potential solutions or components of solutions that address at least one area described in Section D, “Prize Competition Scope.” The submission period for Phase 1 of KidneyX: Redesign Dialysis opens on October 25, 2018. On that date, a webpage for this prize competition will be available on www.kidneyx.org, through which submissions must be made. Complete instructions for submission will be provided on that page.

A participant’s Phase 1 submission (due February 28, 2019), which will be used to determine Phase 1 winners, must be 6 pages or less, 8.5 x 11 inch page, 10-point font or greater and one inch margins. Additionally, participants must include a publicly shareable abstract (not longer than 1 page) describing the proposed solution or component technology. By submitting an entry, all Phase 1 participants automatically agree to allow this abstract to be published on the KidneyX.org site. Participants may, but are not required to, submit a visual supplement as part of their Phase 1 submission (e.g., a link to video, a website, or design specs).

Basis upon which Phase 1 winners will be selected:

A multi-disciplinary judging panel will review submissions for Phase 1 of KidneyX: Redesign Dialysis, and an authorized official will select the winners from the submissions received.

In order to assist the judges in evaluating Phase 1 submissions, participants should ensure that their submission provides sufficient detail and information to allow judges to evaluate the submission in accordance with the following **Phase 1 evaluation criteria**:

- **Potential to significantly improve or add to the landscape of solutions to manage kidney failure.**
 - Clearly demonstrates a vision for medical product development, which should include a clear articulation of the problem being addressed/solved.
 - Clearly demonstrates that the proposed design includes new components, technologies, or approaches that have not previously been part of renal replacement therapies.

- **Nature and extent of anticipated benefit(s) to patients.**
 - Clearly demonstrates efforts to incorporate patient feedback into the design.
 - Clearly addresses one or more of the “Improving Patient Quality of Life” objectives discussed in Section D, above.
- **Feasibility of producing a functional prototype (including scientific and technological rigor).**
 - Clear descriptions of technological or scientific needs, if any, for potential development of a prototype (e.g., what gaps in the proposed solution exist, how might your design fit with existing approaches to create a solution, where do you need additional input?), to better inform and position HHS and ASN to offer assistance if appropriate.
 - Clear explanation of additional challenges or potential pitfalls that need to be considered or addressed.
 - Feasibility of development milestones over one year.
 - Feasibility of regulatory approval of the proposed solution.
 - Clear explanation of the knowledge or expertise the participant/participant team brings to the development of the proposed solution.
- **Quality of evidence supporting the design.**

Phase 2 Submission Requirements:

For Phase 2, participants are asked to demonstrate a prototype solution or component of a solution that addresses at least one area described in Section D, “Prize Competition Scope.” A participant’s Phase 2 submission, which will be used to determine Phase 2 winners, must be 10 pages or less, 8.5 x 11 inch page, 10-point font or greater and one inch margins. Phase 1 winners that wish to participate in Phase 2 must submit a separate Phase 2 application. The participant must also submit a visual (photographic or video) presentation demonstrating the actual prototype. Finally, Phase 2 participants must include a publicly-shareable abstract summary (no more than one page) of the prototype solution. By submitting an entry, Phase 2 participants automatically agree to allow this abstract to be published on the KidneyX.org site.

Basis upon which Phase 2 winners will be selected:

A multi-disciplinary judging panel will review submissions for KidneyX: Redesign Dialysis Phase 2, and an authorized official will select the winners from the submissions received.

In order to assist the judges in evaluating your Phase 2 submission, participants should ensure that their submission provides sufficient detail and information to allow judges to evaluate the submission in accordance with the following **Phase 2 evaluation criteria**:

- **Demonstration of at least the first iteration of a prototype solution whose function addresses one or more elements of the prize competition scope described in Section D, above (testing in animals or humans is not required, but some demonstration or documentation of the prototype’s operating capacity is necessary).**
- **Demonstration of patient input in the design of the prototype.**
 - Degree to which input from patients has informed the development of the prototype.
 - Estimated patient quality of life impact if the prototype solution were to be

- broadly implemented.
- Prototype addresses one or more of the “Improving Patient Quality of Life” objectives discussed in Section D, above.
- **Degree of innovation from past approaches or solutions.**
- **Potential for prototype to significantly advance towards readiness for animal or human studies (if applicable).**
 - Long-term vision for product development of the prototype solution, including potential pathways for commercialization.
 - Collaborations or planned collaborations, if any, with industry or other entities (participants may choose not to disclose all such collaborations if they wish).
 - Next steps and potential challenges envisioned/proposed for product development, potentially including gaps in existing technologies, manufacturing, regulatory, or payment hurdles (the purpose of this information is to better inform and position HHS and ASN to offer assistance if appropriate).

Eligibility Rules:

To be eligible to win a prize under the KidneyX: Redesign Dialysis prize competition, an individual or entity—

- (1) Shall have registered to participate in the prize competition;
- (2) Shall have complied with all the requirements set forth in this announcement for participation in this prize competition;
- (3) For prize money from HHS and/or ASN, who are jointly sponsoring this prize competition - In the case of a private entity, shall be incorporated in and maintain a primary place of business in the United States, and in the case of an individual, whether participating singly or in a group, shall be a citizen or permanent resident of the United States **Note:** Non-U.S. citizens and nonpermanent residents can participate as a member of a team that otherwise satisfies the eligibility criteria but will not be eligible to win a monetary prize (in whole or in part); however, their participation as part of a winning team, if applicable, may be recognized when results are announced;
- (4) May not be a Federal entity or Federal employee acting within the scope of their employment (all non-HHS federal employees must consult with their agency Ethics Official to determine whether the federal ethics rules will limit or prohibit the acceptance of a KidneyX prize);
- (5) Shall not be an HHS employee;
- (6) Federal grantees may not use Federal funds to develop submissions unless consistent with the purpose of their grant award; and
- (7) Federal contractors may not use Federal funds from a contract to develop KidneyX prize competition applications or to fund efforts in support of a KidneyX prize competition submission.

Additional Requirements:

An individual or entity shall not be deemed ineligible because the individual or entity used Federal facilities or consulted with Federal employees during a competition if the facilities and employees are made available to all individuals and entities participating in the competition on an equitable basis.

Each individual (whether participating singly or in a group) or entity agrees to follow all applicable federal, state, and local laws, regulations, and policies.

Participants must also agree to assume any and all risks and waive claims against the Federal Government and its related entities, except in the case of willful misconduct, for any injury, death, damage, or loss of property, revenue, or profits, whether direct, indirect, or consequential, arising from their participation in this prize contest, whether the injury, death, damage, or loss arises through negligence or otherwise.

Participants are not required to obtain liability insurance or demonstrate financial responsibility in any specified amount for claims by a third party for death, bodily injury, or property damage or loss resulting from an activity carried out in connection with participation in a prize competition, but are encouraged to consult with their advisors with respect to the level of insurance that is prudent for each participant. Registered participants agree to indemnify the Federal Government against third party claims for damages arising from or related to prize competition activities, and further indemnify the Federal Government for damage or loss to Government property resulting from such activities.

HHS reserves the right to cancel, suspend, and/or modify this prize competition, or any part of it, for any reason, at HHS's sole discretion. HHS reserves the right not to award any prizes if no entries are deemed worthy. ASN may also discontinue its participation in the prize competition at its discretion. If ASN elects to discontinue its participation, every effort will be made to announce that decision promptly on the KidneyX.org website.

Intellectual Property (IP) Rights:

- Participants are free to discuss their submission and the ideas or technologies that it contains with other parties, are encouraged to share ideas/technologies publicly, are encouraged to collaborate or combine with other teams to strengthen their solutions, and are free to contract with any third parties. Participants should be aware that any agreement signed or obligation undertaken in regard to their participation in this prize competition that conflicts with the prize competition rules, terms, and conditions may result in disqualification of the participant's submission.
- By participating in this prize competition, each participant (whether participating singly or in a group) warrants that he or she is the sole author or owner of, or has the right to use, any copyrightable works that the submission comprises, that the works are wholly original with the participant (or is an improved version of an existing work that the participant has sufficient rights to use and improve), and that the submission does not infringe any copyright or any other rights of any third party of which participant is aware. In addition, each participant (whether participating singly or in a group) and each entity grants to HHS an irrevocable, paid-up, royalty-free nonexclusive worldwide license to reproduce, publish, post, link to, share, and display publicly (e.g., on websites) the submission and abstracts on the web or elsewhere, and a nonexclusive, nontransferable, irrevocable, paid-up license to practice, or have practiced for or on its behalf, the solution throughout the world. Each participant will retain all other intellectual property rights in their submissions, as applicable. To participate in the prize competition, each participant must warrant that there are no legal obstacles to providing the above-referenced

nonexclusive licenses of participant rights to the federal government. To receive an award, participants will not be required to transfer their intellectual property rights to HHS, but participants must grant to the federal government the nonexclusive licenses recited herein. Each participant also warrants that the work is free of security threats and/or malware.

- Each participant must clearly delineate any Intellectual Property (IP) and/or confidential commercial information contained in a submission that the participant wishes to protect as proprietary data.
- All materials submitted to HHS as part of a submission become HHS agency records. Any confidential commercial or financial information contained in a submission must be clearly designated at the time of submission.
- If the submission includes any third party works (such as third party content or open source code), the participant must be able to provide, upon request, documentation of all appropriate licenses and releases for use of such third party works. If the participant cannot provide documentation of all required licenses and releases, HHS and ASN reserve the right, at their sole discretion, to disqualify the submission.

F. Technological and Scientific Needs in Potential Renal Replacement Therapies

This section, drawn directly from the [Kidney Health Initiative's "Technology Roadmap for Innovative Approaches to Renal Replacement Therapy,"](#) details various scientific and technological solutions that would improve or transform renal replacement therapy (RRT). Organized by the various functions that kidneys provide the body, any of the needs listed below could be a topic for a submission in the prize competition. Please do not consider the following list exhaustive: one of this prize competition's goals is to generate as many diverse ideas and solutions as possible.

Kidney Function: Blood Filtration (Filtering blood to remove waste and excess fluid)

Near term needs in blood filtration include:

- Developing a blood filter that allows for filtration/dialysis without the use of anticoagulants; and
- Identifying or generating cell source/type(s) needed to perform desired barrier and permeability functions, and optimize corresponding cell isolation and differentiation techniques (e.g., production of functional glomerular endothelial cells, mesangial cells, and podocyte cells).

Medium term needs in blood filtration include:

- Developing a size-selective, non-clotting blood filter (connected to circulation with or without pump) that is capable of 40 L/day with 12–24 months of continuous performance and will freely pass electrolytes and non-protein-bound toxins.

Longer term needs in blood filtration include:

- Demonstrating function in a full-scale animal model as add-on kidney, followed by support for survival in an anephric animal.

Technical design requirements for products in blood filtration include:

- Non-fouling and able to maintain continuous performance for a period of weeks/months (duration defined by timeframe);
- Generates a filtrate of at least 40L/day (30mL/minute for 24-hour therapy);
- Size selective and able to retain essential blood proteins (e.g., albumin);
- Component materials and design must demonstrate biocompatibility and hemocompatibility; and
- Delivered as sterile to the end user.

Kidney Function: Electrolyte Homeostasis (maintaining appropriate levels of key minerals and ions in the blood). Solutions in this area should normalize and maintain electrolytes (e.g., sodium, potassium, calcium, magnesium, phosphate) within clinically acceptable ranges.

Near term needs in electrolyte homeostasis include:

- Developing a process for passage of filtrate to the engineered structures that contain the differentiated cells.

Medium term needs in electrolyte homeostasis include:

- Generating cells with defined functional characteristics of critical cell types such as 1) proximal tubule (glucose, phosphorus, amino acids, protein, organic ion secretion, bicarbonate, hydrogen ion secretion), 2) distal tubule (magnesium, chlorine, and calcium transport), and 3) collecting duct (proton transport);
- Engineering matrix material and scaffold that will support functional organization and long-term maintenance of the differentiated state of critical cells;
- Developing in-line sensors or point-of-care systems that measure blood and/or effluent electrolytes during RRT treatments to monitor for large variations in blood electrolytes that could lead to symptoms/complications; and
- Developing oral sorbents to augment electrolyte removal.

Longer term needs in electrolyte homeostasis include:

- Developing pores, channels, or ion-selective membranes capable of selective removal or retention of electrolytes (e.g., sodium, potassium, calcium, magnesium, phosphate) from blood filtrate; and
- Demonstrating integrated tubular replacement unit that performs ion transport activities.

Kidney Function: Fluid Regulation (regulating the amount of and/or removing excess fluid). Solutions in this area should have the capacity to remove excess fluid and be adjustable based on the needs of the patient.

Near term needs in fluid regulation include:

- Developing sensors to monitor the intravascular volume status of the patient, allowing for a personalized fluid removal prescription to avoid volume depletion, intradialytic hypotension, and volume overload;
- Developing sensors/methods to measure intra-peritoneal volume in peritoneal dialysis; and

- Generating a cell type/substrate that is water permeable.

Medium term needs in fluid regulation include:

- Demonstrating ex vivo 3D structure with water transport features and permeability characteristics that will allow for net reabsorption of 90%–95% of filtered volume.

Longer term needs in fluid regulation include:

- Developing integrated systems to use sensor input to adjust fluid removal, either by real-time patient adjustment (remote programmable) or as part of a closed-loop system.

Kidney Function: Toxin Removal and Secretion (limiting or preventing toxins in the bloodstream). Solutions should maintain clearance/reduction of the three categories of uremic toxins: 1) small, non-protein bound (clearance of 40L/day); 2) small, protein-bound (reduction in blood concentration); and 3) middle molecules (reduction in blood concentration).

Near term needs in toxin removal and secretion include:

- Generating cell type capable of organic anion/cation transport to secrete protein-bound toxins and drugs that are not freely filtered.

Medium term needs in toxin removal and secretion include:

- Demonstrating an ex vivo 3D structure that exploits filtration and secretion to achieve 70%–90% of normal toxin secretion;
- Developing an RRT system capable of removing each of three categories of “uremic” toxins: (small, non-protein-bound (40L/day clearance); small, protein-bound; middle molecules;
- Developing “smart” filters, mixed-matrix membranes, or blood sorbents capable of binding / adsorbing uremic toxins; and
- Developing oral sorbents capable of binding / adsorbing uremic toxins to augment toxin removal.

Kidney Function: Filtrate Drainage and Connectivity (removing excess filtrate after processing; connectivity issues for filtration, processing, and exterior drainage).

Technical design requirements for products in this area include:

- Composed of biocompatible materials;
- Able to remove unwanted/excess processed filtrate, up to 3L/day;
- Filtrate storage / removal apparatus is acceptable to the patient; and
- Able to handle volume of fluid output with minimal resistance (30mL/minute).

Near term needs in this area include:

- Developing a system for dialysate delivery and removal that is hygienically sound and aesthetically appealing; and
- Developing a filtrate drainage system that is functional, hygienically sound, and aesthetically appealing.

Middle term needs in this area include:

- Creating a highly impermeable conduit (i.e., drainage system from outflow of engineered processing system to exterior, potentially involving the urinary bladder) to move the non-absorbed filtrate from the body.

For optimal RRT treatment, in addition to replicating kidney functions, there is need for improved RRT access (vascular, peritoneal, or blood circuit access needed for treatment).

Near term needs in improved RRT access include:

- Developing components of the blood circuit that allow for hemodialysis without the need for systemic anticoagulation;
- Developing a 3D scaffold or membrane device capable of vascular oxygenation and nutrient access for transporting epithelial cells and demonstrate activity ex vivo; and
- Developing PD access with reduced risk of infection.

Medium term needs in improved RRT access include:

- Developing technologies that detect a vascular access disconnect and/or act to avoid blood loss in the event of a disconnect (e.g., a sensor that integrates with machine software to stop the blood pump and put hemodialysis machine in safe mode);
- Developing a safer vascular access capable of preventing (e.g., needle-free) or mitigating (e.g., self-sealing) catastrophic events of a vascular access disconnect;
- Developing access that is non-intrusive and functionally acceptable, easy and quick for the patient to connect and disconnect, secure with minimal discomfort (e.g., skin-level or sub-cutaneous access), and aesthetically pleasing to patients; and
- Demonstrating a mechanism for reabsorbed fluid and electrolytes to enter the circulation.

Longer term needs in improved RRT access include:

- Developing a vascular access for hemodialysis that makes it easier for patients to connect and disconnect from the hemodialysis machine (ideally, the access would be needle-free and reduce the risk of vascular-access-related bloodstream infections and other complications, e.g., fibrin sheath, venous stenosis);
- Developing an entire blood circuit that allows for hemodialysis without the need for systemic anticoagulation;
- Developing a vascular access with internal connection to the native vasculature that maintains patency without the need for systemic anticoagulation;
- Developing vascular access that significantly reduces the risk of infection over the life of the implant; and
- Recruiting host vessels to implanted add-on kidney and demonstrate perfusion of implanted tissue that is sufficient to maintain cell health and physiological functions.

There are also ancillary technologies that will be vital to improving RRT.

Near term needs in ancillary technologies include:

- Developing lightweight rechargeable batteries capable of powering RRT systems; and
- Developing miniaturized systems (e.g., sorbents) capable of regenerating spent dialysate.

Long term needs in ancillary technologies include:

- Developing blood / filtrate / dialysate pumps that are miniaturized, low-energy, and hemocompatible;
- Developing lightweight power source capable of powering RRT systems that can be recharged using wireless energy transfer; and
- Developing miniaturized efficient systems to generate sterile water for replacement fluid / dialysate generation.

Finally, an improved RRT will need safety monitoring functions.

Near term needs in safety monitoring include:

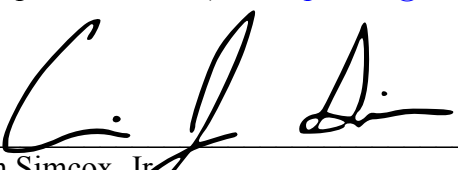
- Developing technologies to allow real-time treatment monitoring of various sensors (flow, pressure, volume status, electrolytes, etc.) that can be observed/tracked by patients and providers;
- Developing online ammonia / saturation sensors to alert users that sorbent cartridges need to be replaced;
- Standardizing panel of immune markers to assess tolerance of RRT product (i.e., minimize immune rejection);
- Identifying in vitro surrogate assays or biomarkers for assessing safety and proper functioning of the RRT; and
- Developing sensors that can provide feedback on output fluid volume and blood concentrations of key components (e.g., potassium, sodium, calcium, phosphorus, pH).

Longer term needs in safety monitoring include:

- Developing sensors that monitor the integrity of the biological product itself (i.e., when to replace cells);
- Developing integrated systems that use sensor input to allow adjustment in real-time or as part of a closed-loop system; and
- Conducting in vivo testing to evaluate safety (e.g., toxicity), integrity, longevity, and tolerance of RRT product.

For Further Information Contact:

Ross Bowling, Ph.D. (Ross.Bowling@hhs.gov, 202-260-7158) or
Sandeep Patel, Ph.D. (Sandeep.Patel@hhs.gov, 202-205-0355).



Edwin Simcox, Jr.
Chief Technology Officer

9/26/18

Date